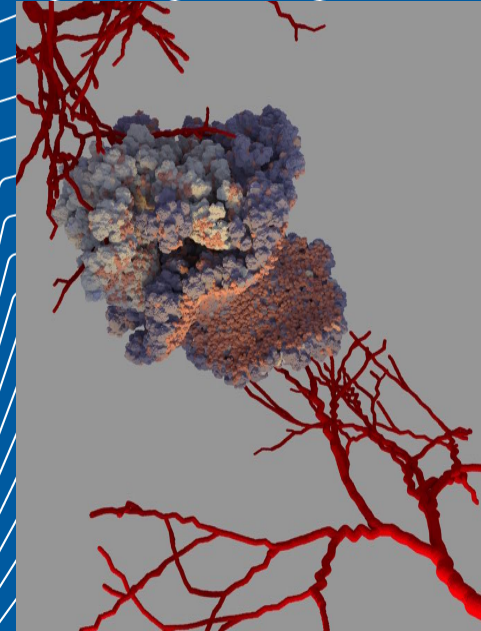


MASSIVELY PARALLEL LARGE-SCALE MULTI-MODEL SIMULATION OF TUMOR DEVELOPMENT INCLUDING TREATMENTS

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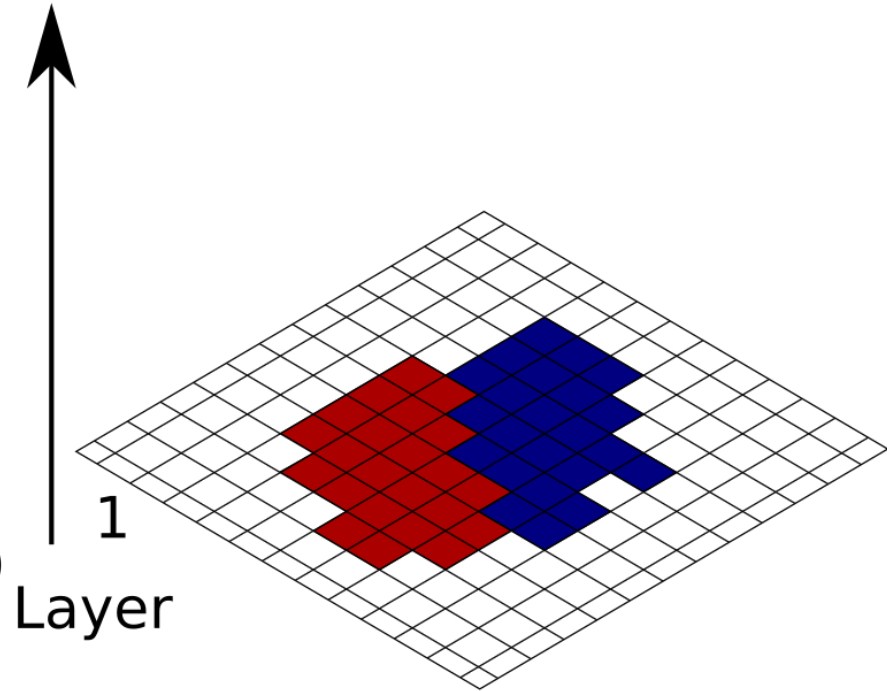


MULTI LEVEL – MULTI SCALE

Cellular Potts Model (microscale)

- Grid based cell dynamics simulation
- Graner, François; Glazier, James (1992)
- Metropolis Monte Carlo acceptance of new states based on H_{CPM}
- Mostly applied in 2D

$$\begin{aligned} H_{\text{CPM}} = & \sum_{\sigma \in \text{cells}} \lambda_V (V(\sigma) - V_0(\sigma))^2 \\ & + \sum_{\sigma \in \text{cells}} \lambda_S (S(\sigma) - S_0(\sigma))^2 \\ & + \sum_{x \in \text{voxels}} \sum_{x' \in \text{neighbors}} J_{\tau(\sigma(x))\tau(\sigma(x'))} (1 - \delta_{\sigma(x)\sigma(x')}) \\ & + \dots \end{aligned}$$



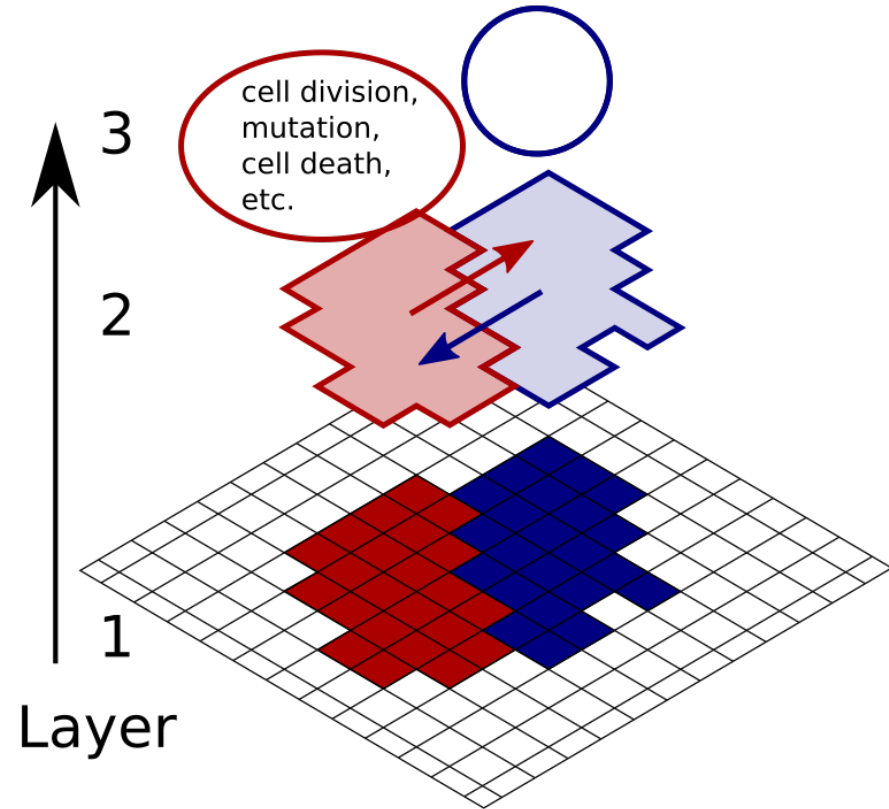
MULTI LEVEL – MULTI SCALE

Agent based (macroscale)

- Properties on cell level
- Signaling (drugs, nutrient)
- Processing of signals
- Cell division

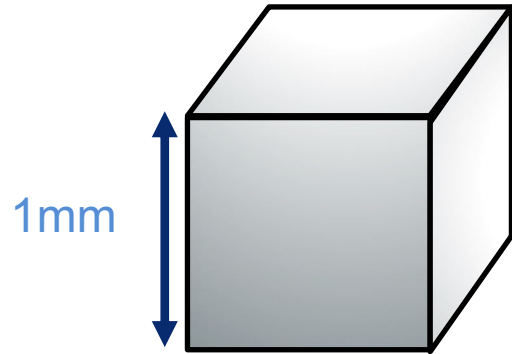
In between (mesoscale)

- Diffusion of signals
- According to the surface of cells

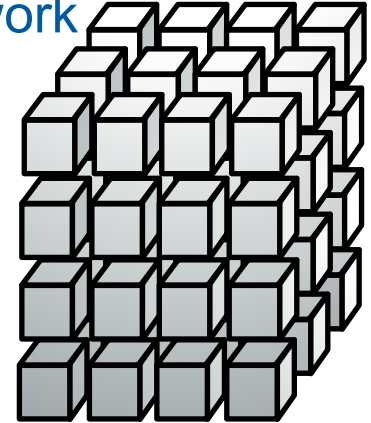


PARALLELIZATION

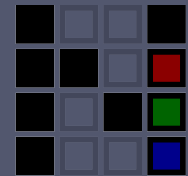
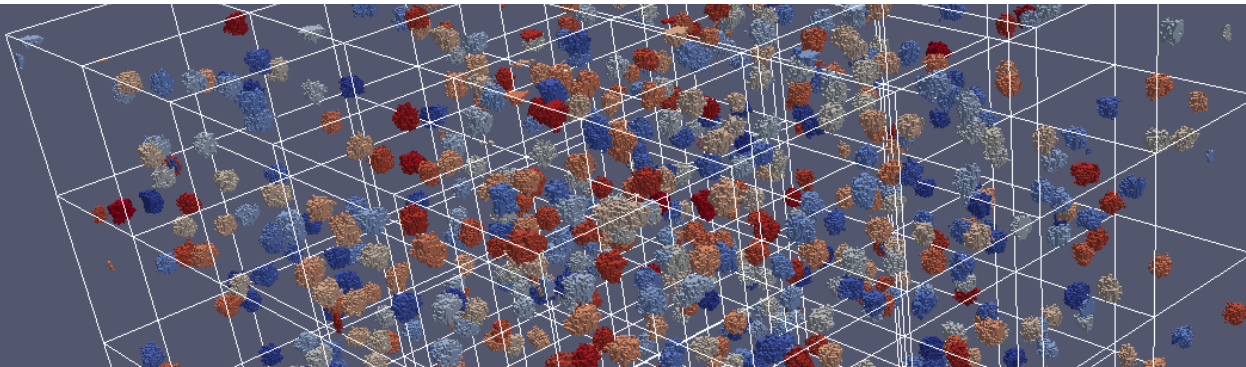
MPI parallelization in newly developed simulation framework



~ 10^6 cells
~ 1000 cores
(100 block size)

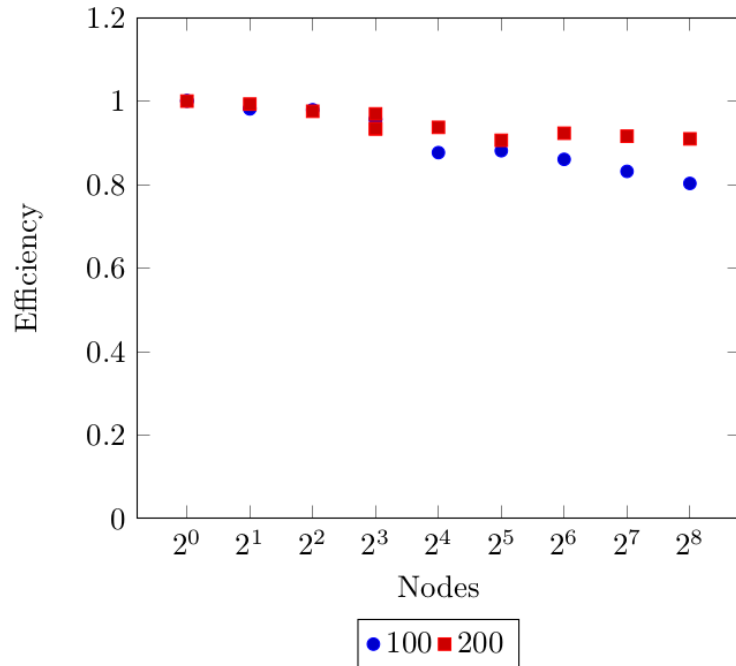


[Berghoff et al. "Massively parallel stencil code solver with autonomous adaptive block distribution." *IEEE Transactions on Parallel and Distributed Systems* 29(10) 2018.]



NASTJA

EXCELLENT SCALING



Summary of Cell Simulation in the NASTJA-Framework

Parallel Cell Simulations

- up to 1 million cells
- 1 billion DoF

CPM

- modular in energy contributions

Modular actions

- Division,
- Mutation,
- Death, ...

General signaling

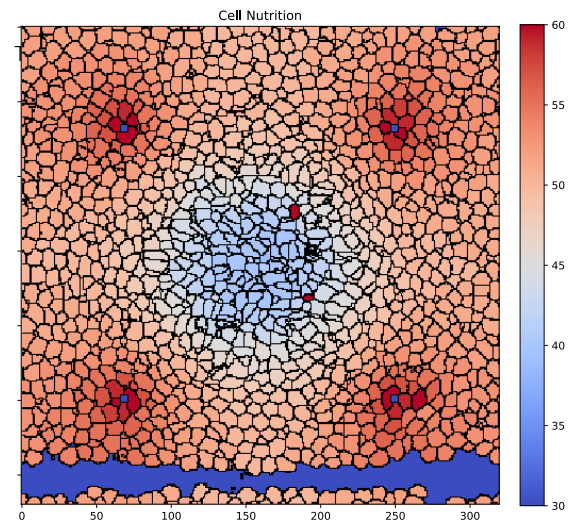
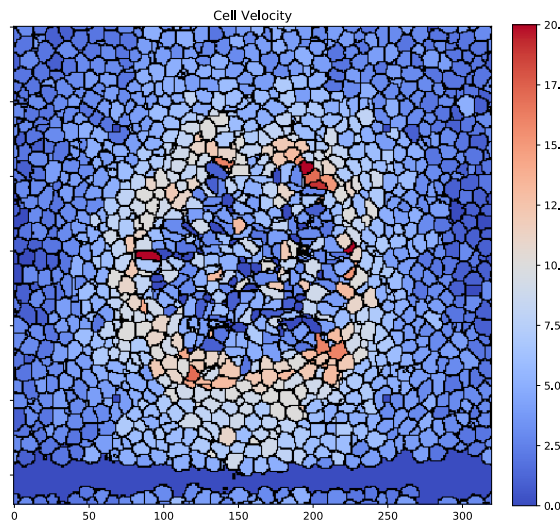
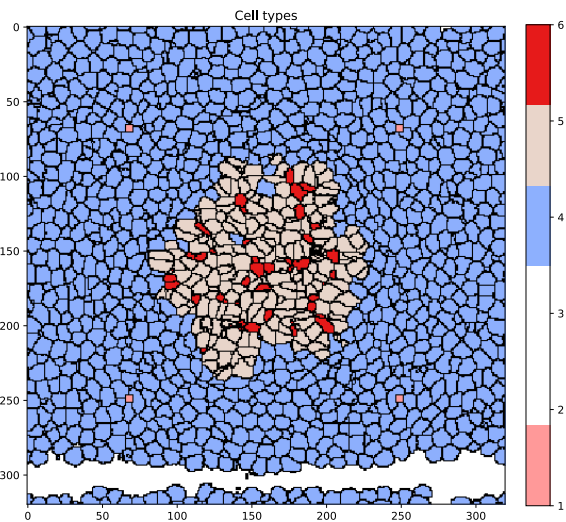
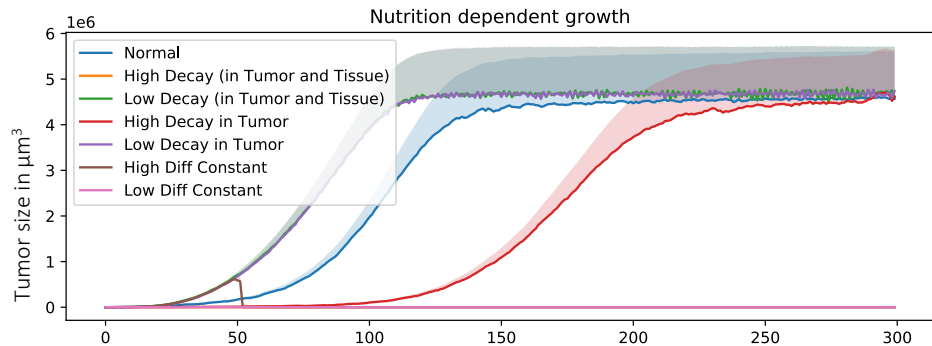
- Nutrients,
- Drugs, ...

APPLICATIONS

MODELING TUMOR GROWTH

Nutrient transport

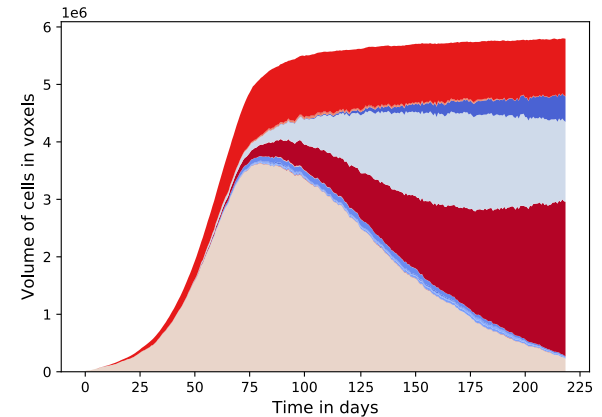
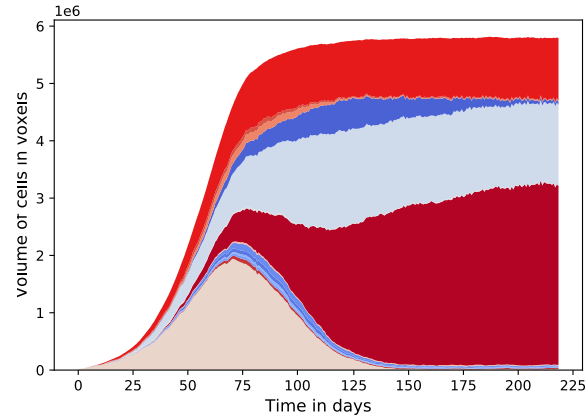
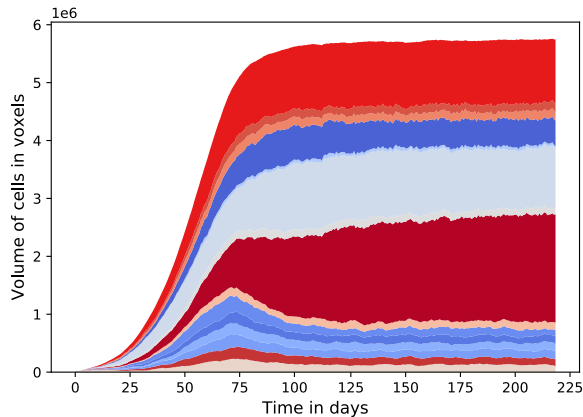
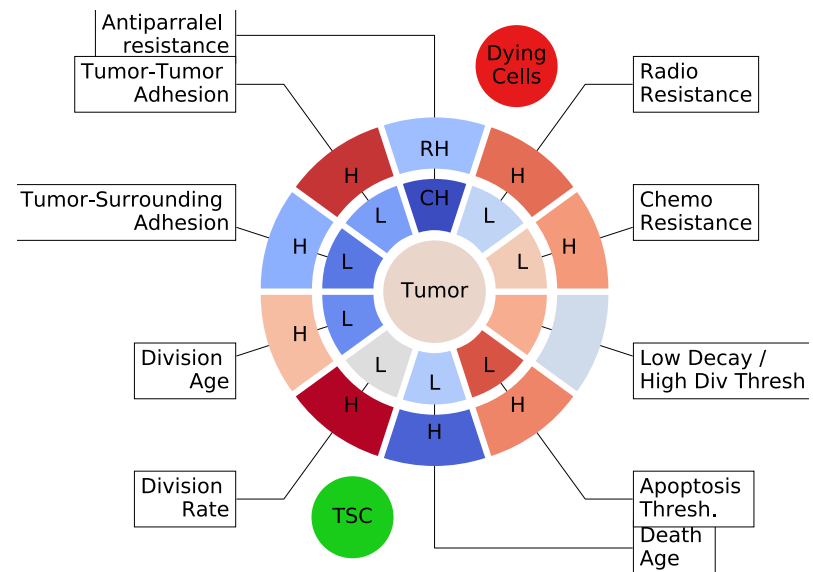
- Nutrient transport from bloodvessels
- Celldivision dependant on nutrition
- Necrosis can be induced



TUMOR HETEROGENEITY

Evolution of tumor cell type composition

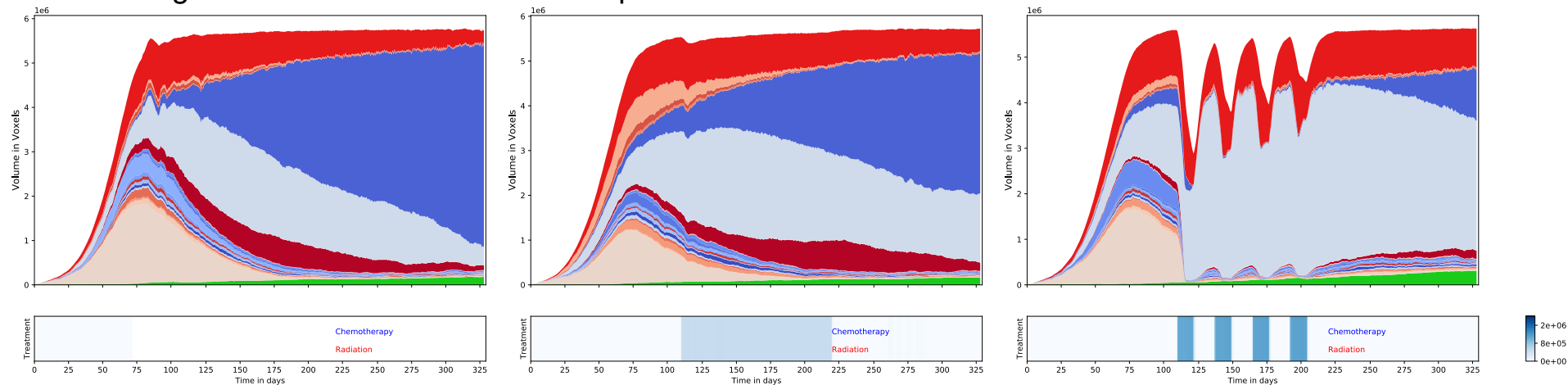
- N different tumor cell types with varying parametrization
- Mutation events occur at cell division
- Same mutation probability between all cell types:
- mutate every 200, 20, 2 divisions



TREATMENT MODELS

External suppression of cell division and death chemo- and radiotherapy

- Chemotherapy modeling
- Chemotherapy signal inhibits cell division
- Testing different treatment models and protocols



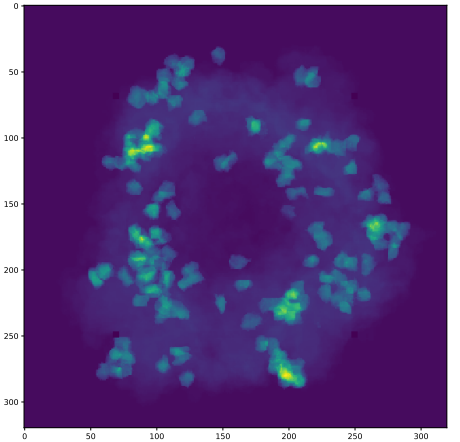
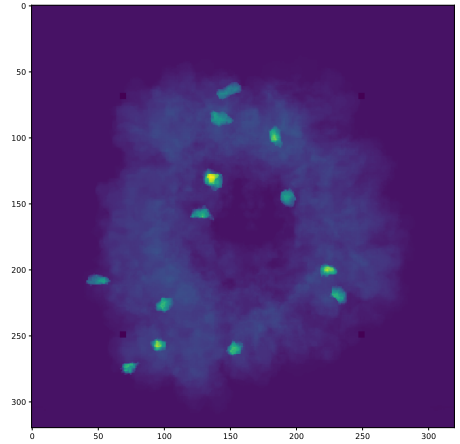
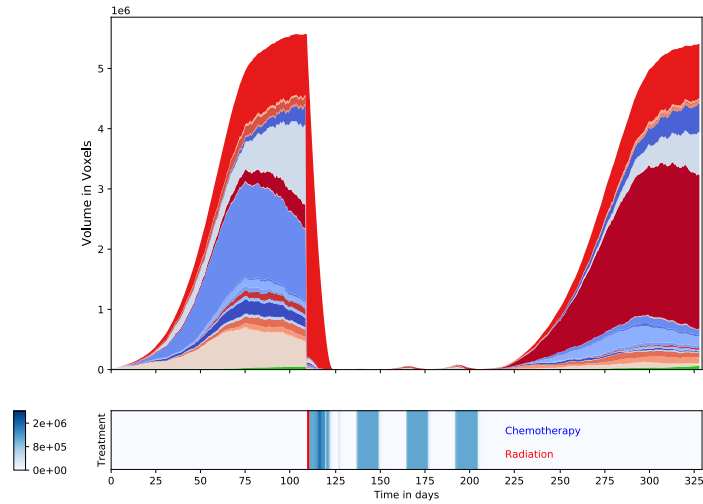
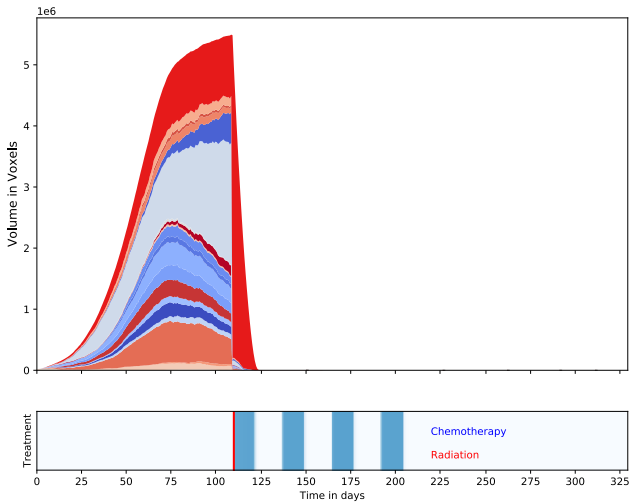
Chemotherapy

- Radiation induces cell death and alters division rates

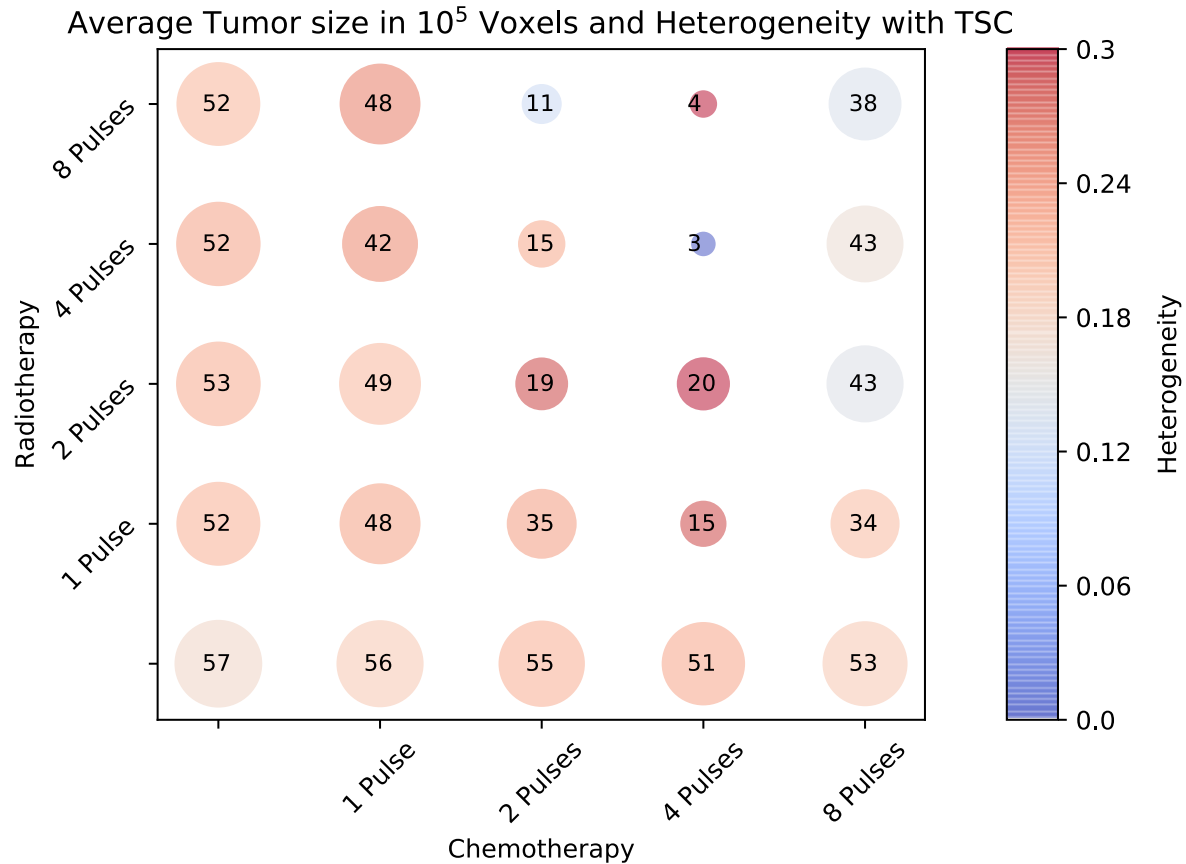
TUMOR STEM CELLS

Evolution of tumor cell type composition

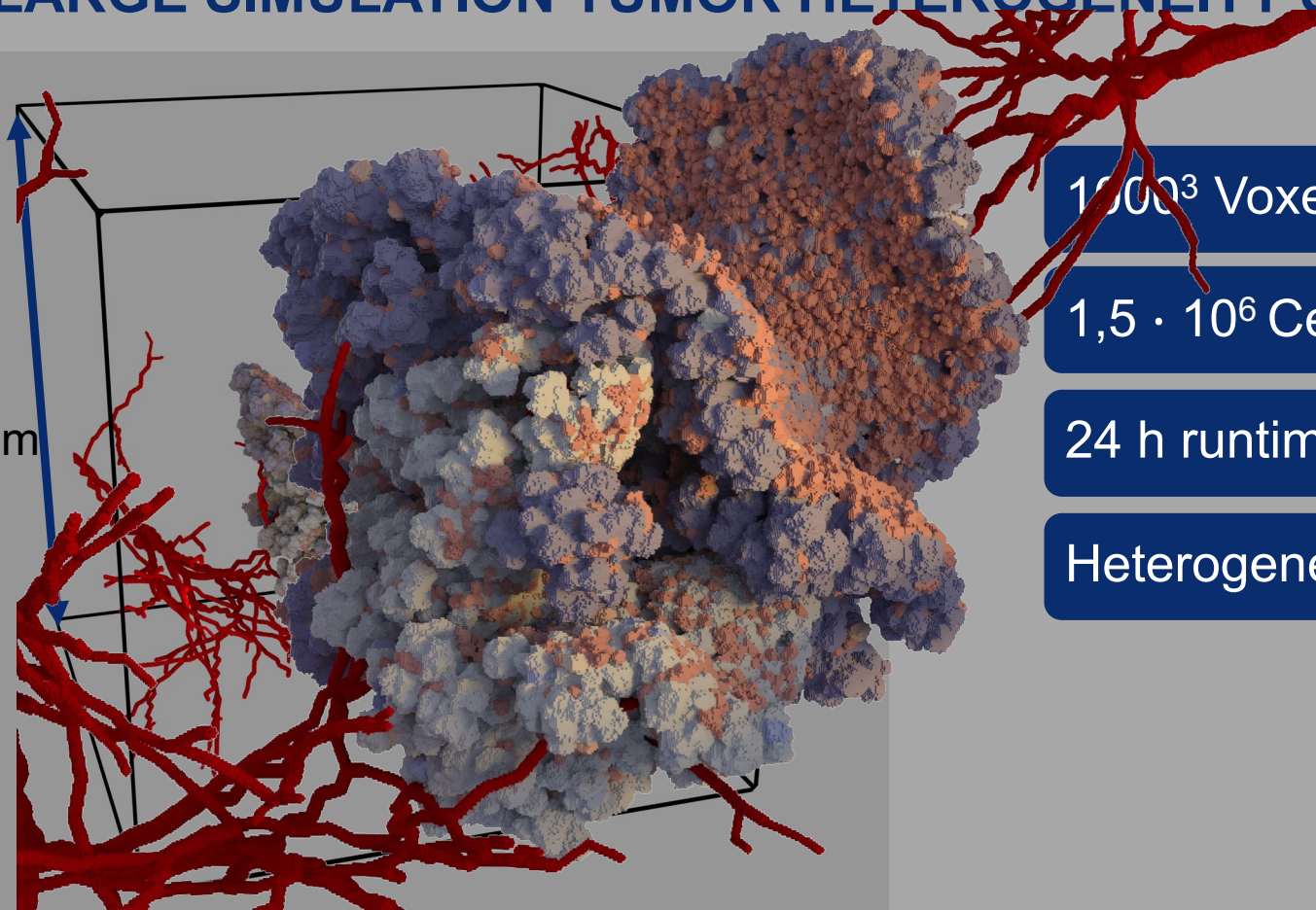
- Slower cell cycle
- Asymmetric division into tumor cell and TSC



TREATMENT RESPONSE



LARGE SIMULATION TUMOR HETEROGENEITY SIMULATION



1000^3 Voxels

$1,5 \cdot 10^6$ Cells

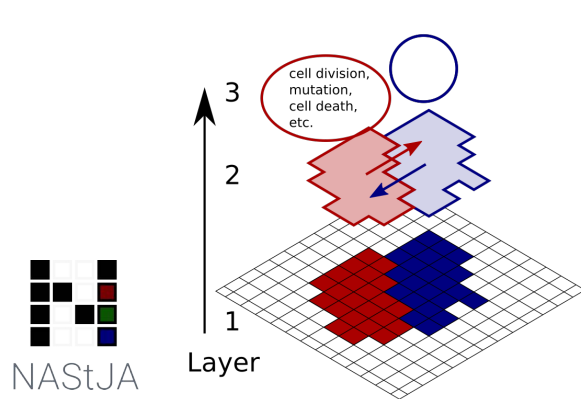
24 h runtime on JURECA

Heterogeneity enabled

SUMMARY

Features

- Modular structure of the model and energy terms
- Excellent scaling -> 10^6 s of cells
- Multiscale: mm scale simulations at μm resolution
- Cell-to-cell signaling
- Agent based layer for cell properties



Applications

- Tumor development
- Heterogeneity
- TSC
- Treatment response

